

FORM PTO-1449

INFORMATION DISCLOSURE CITATIONAttorney Docket  
23138A-TSerial Number  
Not yet assigned

Applicant

STEINER et al.

Filing Date  
June , 2001Group Art Unit  
161409/879888  
U.S. PTO

06/14/01

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Examiner Initial		Document Number	Date	Name	Class	Sub-Class	Filing Date
<i>h</i>	AA	5,532,248	7/2/96	Goulet et al.			5/12/95
	AB	5,506,228	4/9/96	Norton et al.			2/23/95
	AC	5,470,878	11/28/95	Michnick et al.			12/8/93
	AD	5,457,111	10/10/95	Luly et al.			11/9/93
	AE	5,385,918	1/31/95	Connell et al.			2/9/93
	AF	5,342,625	8/30/94	Hauer et al.			12/15/92
	AG	5,292,747	3/8/94	Davis et al.			9/21/92
	AH	5,284,877	2/8/94	Organ et al.			6/12/92
	AI	5,284,840	2/8/94	Rupprecht et al.			6/12/92
	AJ	5,284,826	2/8/84	Eberle			8/27/92
<i>h</i>	AK	5,258,389	11/2/93	Goulet et al.			11/9/92

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		Document Number	Date	Country	Class	Sub-Class	Translation
<i>h</i>	AL	WO/9641609	12/27/96	US PCT-			Yes
	AM	EP 564924	10/13/93	EP			Yes
	AN	EP 423714	4/24/91	EP			Yes
<i>h</i>	AO	WO 9736869	10/9/97	US PCT			Yes

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>h</i>	AP		Birkenshaw, T.N. et al., "Synthetic FKBP12 Ligands. Design and Synthesis of Pyranose Replacements," <u>Bioorganic &amp; Medicinal Chemistry Letters</u> , (1994) 4:21, 2501-2506.
	AQ		Caffrey, M.V. et al., "Synthesis and Evaluation of Dual Domain Macrocyclic FKBP12 Ligands," <u>Bioorganic &amp; Medicinal Chemistry Letters</u> , (1994) 4:21, 2507-2510.
<i>h</i>	AR		Hauske, J.R. et al. "Design and Synthesis of Novel FKBP Inhibitors," <u>J. of Medicinal Chemistry</u> , (1992) 35, 4284-4296.

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Examiner Initial		Document Number	Date	Name	Class	Sub-Class	Filing Date
M	BA	5,208,241	5/4/93	Ok et al.			9/9/91
	BB	5,192,773	3/9/93	Armistead et al.			7/2/90
	BC	5,189,042	2/23/93	Goulet et al.			8/22/91
	BD	4,996,193	2/26/91	Hewitt et al.			3/3/89
u	BE	5,614,547	3/25/97	Hamilton et al.			6/7/95

**FOREIGN PATENT DOCUMENTS**

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							Yes No
							Yes No
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							Yes No

**OTHER (Including Author, Title, Date, Pertinent Pages, etc.)**

M	BF		Holt, D.A. et al., "Design, Synthesis, and Kinetic Evaluation of High-Affinity FKBP Ligands and the X-ray Crystal Structures of Their Complexes with FKBP12," <u>J. Am. Chem. Soc.</u> , (1993) 115, 9925-9938.
	BG		Holt, D.A. et al., "Structure-Activity Studies of Synthetic FKBP Ligands as Peptidyl-prolyl Isomers Inhibitors," <u>Bioorganic &amp; Medicinal Chemistry Letters</u> , (1994) 4:2, 315-320.
N	BH		Holt, D.A. et al., "Structure-Activity Studies of Nonmacrocylic Rapamycin Derivatives," <u>Bioorganic &amp; Medicinal Chemistry Letter</u> , (1993) 3:10, 1977-1980.

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	CA	Luengo, J.I. et al., "Synthesis and Structure-Activity Relationships of Macrocyclic FKBP Ligands," <u>Bioorganic &amp; Medicinal Chemistry Letters</u> , (1994) 4:2, 321-324.
	CB	Snyder, S.H. et al., "Immunophilins and the Nervous System," <u>Nature Medicine</u> , (1995) 1:1, 32-37.
	CC	Teague, S.J. et al., "Synthesis and Study of a Non-Macrocyclic FK506 Derivative," <u>Bioorganic &amp; Medicinal Chemistry Letters</u> , (1994) 4:13, 1581-1584.
	CD	Steiner, et al., <u>Chemical Abstract</u> , Volume 126:272710, 1997.

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<i>N</i>	DA	Teague, S.J. et al., "The Affinity of the Excised Binding Domain of FK-506 for the Immunophilin FKBP12," <u>Bioorganic &amp; Medicinal Chemistry Letters</u> , (1993) 3:10, 1947-1950.
<i>N</i>	DB	Wang, G.T. et al., "Synthesis and FKBP Binding of Small Molecule Mimics of the Tricarbonyl Region of FK506," <u>Bioorganic and Medicinal Chemistry Letters</u> , (1994) 4:9, 1161-1166.
<i>N</i>	DC	Yamashita, D.S. et al., "Design, Synthesis and Evaluation of Dual Domain FKBP Ligands," <u>Bioorganic &amp; Medicinal Chemistry</u> , (1994) 4:2, 325-328.

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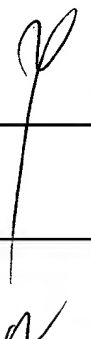

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	EA	Iwabuchi, T. et al., "Effects of immunosuppressive peptidyl-prolyl cis-trans isomerase (PPIase inhibitors, cyclosporin A, FK506, ascomycin and rapamycin, on hair growth initiation in mouse: immunosuppression is not required for hair growth," <u>J. of Dermatol. Sci.</u> , (1995) 9:1, 64-69.
	EB	Yamamoto, S. et al., "Stimulation of hair growth by topical application of FK506, a potent immunosuppressive agent," <u>J. Invest. Dermatol.</u> , (1994) 102:2, 160-164.
	EC	Jiang, H. et al., "Induction of anagen in telogen mouse skin by topical application of FK506, a potent immunosuppressant," <u>J. Invest. Dermatol.</u> , (1995) 104:4, 523-525.

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<i>W</i>	FA	5,447,915	9/5/95	Schreiber et al.			8/28/92
	FB	5,294,603	3/15/94	Rinehart, K.L.			2/18/92
	FC	5,359,138	10/25/94	Takeuchi et al.			6/29/92
<i>N</i>	FD	5,516,797	5/14/96	Armistead et al.			4/11/94

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<i>N</i>	FE	WO9203472	3/5/92	<i>WG</i> - PET			Yes
	FF	JP04149166	5/22/92	<i>JP</i> Japan			No
	FG	EP-468339	1/29/92	<i>EP</i>			Yes
	FH	WO9113088	9/5/91	<i>WD</i> - PET			Yes
	FI	EP-405994	1/2/91	<i>EP</i>			Yes
<i>N</i>	FJ	EP-378318	7/18/90	<i>EP</i>			Yes

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>M</i>	FK	Askin, D. et al., "Effecient Degradation of FK-506 to a versatile synthetic intermediate," J. Org. Chem., 1990, 55(20), 5451-4.
	FL	Goulet, Mark T., and Boger, Joshua, "Degradative studies on the tricarbonyl containing macrolide rapamycin," Tetrahedron Lett., 1990, 31(34), 4845-8.
	FM	Jones, T. et al., "Chemistry of tricarbonyl hemiketals and application of Evans technology to the total synthesis of the immunosuppressant (-)-FK-506," J. Am. Chem. Soc., 1990, 112(8), 2998-3017.
	FN	Jones, A. et al., "A formal synthesis of FK-506. Exploration of some alternatives to macrolactamization," J. Org. Chem., 1990, 55(9), 2786-97.
	FO	Rao, A.V., et al., "Studies directed towards the synthesis of immunosuppressive agent FK-506: construction of the tricarbonyl moiety," Tetrahedron Lett., 1990, 31(10), 1439-42.
<i>N</i>	FP	Harding, M.W., et al., "A receptor for the immunosuppressant FK506 is a <i>cis-trans</i> peptidyl-prolyl isomerase," Nature Lett., 1989, 341, 758-60.

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<i>W</i>	GA	4,818,749	4/4/89	Gold, E.H. et al.			4/4/89
	GB	4,808,573	2/28/89	Gold, E.H. et al.			2/28/89
	GC	5,252,579	10/12/93	Skotnicki, J. et al.			2/16/93
<i>A</i>	GD	5,543,423	8/6/96	Zelle et al.			1/23/95

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<i>W</i>	GE	WO9104985	4/18/91	WO PCT			Yes
	GF	DE4015255	11/14/91	DE Germany			No
	GG	EP-419049	3/27/91	EP			Yes
	GH	WO9012805	11/1/90	WO PCT			No
	GI	EP-352000	1/24/90	EP			Yes
	GJ	DE3931051	3/29/90	DE Germany			No
<i>W</i>	GK	EP-333174	9/20/89	EP			Yes

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>W</i>	GL	Finberg, Robert W. et al., "Prevention of HIV-1 Infection and Preservation of CD4 Function by the Binding of CPFs to gp120," Science, 1990, 249, 287-91.
<i>W</i>	GM	Goodfellow, Val S. et al., "p-Nitrophenyl 3-diazopyruvate and diazopyruvamides, a New Family of Photoactivatable Cross-Linking Bioprobes," Biochemistry, 28(15), 6346-60.
	GN	<del>Wasserman, H.H. et al., "Synthesis of the tricarbonyl region of FK-506 through an amidophosphorane [Erratum to document cited in CA111(7):57366p], " J. Org. Chem., 1989, 54(22), 5406.</del>
<i>W</i>	GO	Wasserman, H.H. et al., "Synthesis of the tricarbonyl region of FK-506 through an amidosphere," J. Org. Chem., 1989, 54(12), 2785-6.
	GP	Askin, D. et al., "Chemistry of FK-506: benzilic acid rearrangement of the tricarbonyl system," Tetrahedron Lett., 1989, 30(6), 671-4.
<i>W</i>	GQ	Coleman, R., and Danishefsky, S., "Degradation and manipulations of the immunosuppressant FK506: preparation of potential synthetic intermediates," Heterocycles, 1989, 28(1), 157-61.

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HA		4,574,079	3/4/86	Gavras, H.P. et al.			3/4/86
HB		5,330,993	7/19/94	Armistead, et al.			7/2/91

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HC		WO8809789	12/15/88	WO PCT			Yes
HD		EP-260118	3/16/88	EPO			Yes
HE		WO9617816	6/13/96	WO PCT			Yes

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HF		Boulmedais, Ali et al., "Stereochemistry of Electrochemical Reduction of Optically Active $\alpha$ -ketoamides. II. Electroreduction of benzoylformamides derived from S-(-)-proline," Bull. Soc. Chim. Fr., 1989, (2), 185-91. (French)	
HG		Soai, Kenso et al., "Asymmetric Allylation of $\alpha$ -keto amides Derived from (S)-proline esters," Pept. Chem., 1986, 24, 327-330.	
HH			
HJ		Egbertson, M. and Danishefsky, S., "A synthetic route to the tricarboxyl region of FK-506," J. Org. Chem., 1989, 54(1), 11-12.	
HK		Williams, D.R. and Benbow, J.W., "Synthesis of the $\alpha,\beta$ diketo amide segment of the novel immunosuppressive FK506," J. Org. Chem., 1988, 53(191), 4643-4.	
HL		Kocienski, P. et al., "A synthesis of the C(1)-C(15) segment of tsukubaenolide (FK506)," Tetrahedron Lett., 1988, 29(35), 4481-4.	
HM		Tanaka, H. et al., "Structure of FK506, a novel immunosuppressant isolated from Streptomyces," J. Am. Chem. Soc., 1987, 109(16), 5031-3.	

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<i>N</i>	IA	4,374,829	2/22/83	Harris, E.E. et al.			2/22/83
	IB	5,147,877	9/15/92	Goulet, Mark			9/12/91

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	IC	EP-196841	10/8/86	EP			Yes
	ID	DE3508251	9/11/86	DE Germany			No
	IE	EP--88350	9/14/83	EP			Yes
<i>N</i>	IF	EP--73143	3/2/83	EP			Yes

**OTHER (Including Author, Title, Date, Pertinent Pages, etc.)**

<i>N</i>	IG		Soai, Kenso and Ishizaki, Miyuki, "Asymmetric Synthesis of Functionalized tertiary alcohols by diastereoselective allylation of chiral $\alpha$ -keto amides derived from (S)-proline esters: control of stereochemistry based on saturated coordination of Lewis acid," J. Org. Chem., 1986, 57(17) 3290-5. (English)
	IH		Soai, Kenso et al., "Asymmetric synthesis of both enantiomers of $\alpha$ -hydroxy acids by the diastereoselective reduction of chiral $\alpha$ -keto amides with complex metal hydrides in the presence of a metal salt," Chem. Lett., 1986, 11, 1897-900.
	II		Soai, Kenso and Hasegawa, Hitoshi, "Diastereoselective reduction of chiral $\alpha$ -ketoamides derived from (S)-proline esters with sodium borohydride. Preparation of optically active $\alpha$ -hydroxy acids," J. Chem. Soc., 1985, 1(4), 769-72.
<i>N</i>	IJ		Soai, Kenso and Ishizaki, Miyuki, "Diastereoselective asymmetric allylation of chiral $\alpha$ -keto amides with allyltrimethylsilane. Preparation of protected homoallylic alcohols," J. Chem. Soc., 1984, 15, 1016-1017.
	IK		
<i>N</i>	IL		Bender, D., et al., "Periodate oxidation of $\alpha$ -keto $\gamma$ -lactams. Enol oxidation and $\beta$ -lactam formation. Mechanism of periodate hydroxylation reactions," J. Org. Chem., 1978, 43(17), 3354-62.

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<i>W</i>	JA	5,631,017	5/20/97	Sharpe, et al.		<i>X</i>	3/26/93
	JB	5,703,088	12/30/97	Sharpe, et al.		<i>X</i>	6/4/92

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	JC	EP--50800	5/5/82	EPO		<i>X</i>	Yes
	JD	EP--48159	3/24/82	EPO		<i>X</i>	Yes
<i>W</i>	JE	EP--12401	6/25/80	EPO		<i>X</i>	Yes

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<i>W</i>	JF		Colombo, L. et al., "Enantioselective synthesis of secondary alcohols in the presence of chiral ligands," Tetrahedron, 1982, 38(17), 2725-7.
	JG		Soai, Kenso et al., " <del>Unusual</del> effect of a mixed solvent on the asymmetric reduction of chiral $\alpha$ -keto amides with sodium borohydride," J. Chem. Soc., 1982, 21, 1282-3.
<i>W</i>	JH		Steglich, Wolfgang et al., "Activated carboxylic acid derivatives. II. A simple synthesis of 2-oxycarboxylic acid amides, N-(2-oxoacyl)amino acid esters and 2-oxocarboxylic acid hydrazides," Synthesis, 1978, 8, 622-4. (German)
	JI		Cushman, D.W. et al., "Design of potent competitive inhibitors of angiotensin-converting enzyme. Carboxyalkanoyl and mercaptoalkanoyl amino acids," Biochemistry, 1977, 16(25), 5484-91.
<i>W</i>	JJ		Steglich, Wolfgang and Hinze, Sabine, "A rational synthesis of N-trifluoroacetyl amino acids," Synthesis, 1976, 8, 399-401. (German)
	JK		<del>_____</del>
<i>W</i>	JL		Marshall, J.A. et al., "Convenient synthesis of dioxopiperazines via aminolysis of $\alpha$ -(pyruvylamino) esters, Synth. Commun., 1975, 5(3), 237-44.
	JM		Haeusler, Johannes and Schmidt, Ulrich, "Amino acids and peptides. IX. Pyruvoyl amino acids," Chem. Ber., 1974, 107(1), 145-51. (German)
<i>W</i>	JN		Hearn, Walter R., and Worthington, Robert E., "L-Proline-N-oxalic anhydride," J. Org. Chem., 1967, 32(12), 4072-4.

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U	KA	5,424,454	6/13/95	Burbaum, B.W. et al.			5/26/94
	KB	5,319,098	6/7/94	Burbaum, B.W et al.			5/18/93

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	KC	WO9200278	1/9/92	WO PCT			Yes
	KD	WO9606097	2/29/96	WO PCT			Yes
	KE	WO9512572	5/11/95	WO PCT			Yes
	KF	WO9407858	4/14/94	WO PCT			Yes
	KG	WO9325546	12/23/93	WO PCT			Yes
	KH	WO9313066	7/8/93	WO PCT			Yes
	KI	JP05178824	7/20/93	JP Japan			No
	KJ	EP-572365	12/1/93	EP			Yes
	KK	WO9219593	11/12/92	WO PCT			Yes
	KL	GB2247456	3/4/92	GB United Kingdom			Yes
	KM	WO9218478	10/29/92	PCT			Yes

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W	KN	Chakarabarty, Tushar K., "Studies towards the development of cyclic peptide-based analogs of macrolide immunosuppressants," Pure Appl. Chem., 1996, 68(3), 565-568.
	KO	
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U	KQ	Tugwell, Peter, "Clycospurin in the Treatment of Rheumatoid Arthritis," J. of Autoimmunity, 1992, 5, 231-40.
	KR	Fry, Lionel, "Psoriasis: Immunopathology and Long-term treatment with Cyclosporin," J. of Autoimmunity, 1992, 5, 277-83.
U	KS	Feutren, Gilles, "The Optimal use of Cyclosporin A in Autoimmune Diseases," J. of Autoimmunity, 1992, 5, 183-95.

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<i>W</i>	LC	EP-652229	5/10/95	EP			Yes
<i>W</i>	LD	ZA9207782	4/28/93	South Africa			Yes

**OTHER (Including Author, Title, Date, Pertinent Pages, etc.)**

<i>W</i>	LE		Slee, Deborah H. et al., "Selectivity in the Inhibition of HIV and FIV Protease: Inhibitory and Mechanistic Studies of Pyrrolidine-Containing $\alpha$ -Keto Amide and Hydroxyethylamine Core Structures, J. Am. Chem. Soc., 1995, 117(48), 1187-78.
	LF		Nicolaou, K.C. et al., "Total synthesis of rapamycin," Che.--Eur. J., 1995, 1(5), 318-33.
<i>W</i>	LG		Munoz, Benito et al., " $\alpha$ -Ketoamide Phe-Pro isostere as a new core structure for the inhibition of HIV protease," Bioorg. Med. Chem., 1994, 2(10), 1085-90.
	LH		Hauske, James R. et al., "Investigation of the effects of synthetic, non-cytotoxic immunophilin inhibitors on MDR," Bioorg. Med. Chem. Lett., 1994, 4(17), 2097-102.
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	LJ		Ranganathan, Darshan et al., "Protein Backbone Modification by Novel C $\alpha$ -C Side-Chain Scission," 1994, J. Am. Chem. Soc., 116(15), 6545-57.
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	LM		Karle, Isabella L. et al., "Coformation of the oxalamide group in retro-bispeptides. Three crystal structures," Int. J. Pept. Protein Res., 1994, 43(2), 160-5.
<i>W</i>	LN		Kaczmar, et al., Makromol. Chem., 1976, 177, 1981-9 (German).

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FORM PTO-1449

INFORMATION DISCLOSURE CITATIONAttorney Docket  
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MB						

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✓	MC <del>W</del> 9405639	3/17/94	WO PCT			Yes
✓	MD <del>W</del> 9615101	5/23/96	WO PCT			Yes

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✓	ME	Steiner, Joseph P. et al., "High brain densities of the immunophilin FKBP colocalized with calcineurin," Nature Lett., 1992, 358, 584-7.
	MF	Pattenden, Gerald and Tankard, Mark, "Facile Synthesis of the tricarbonyl subunit in the immunosuppressant rapamycin," Tetrahedron Lett., 1993, 34(16), 2677-80.
	MG	Furber, M. et al., "Studies relating to the immunosuppressive activity of FK506," Tetrahedron Lett., 1993, 34(8), 1351-4.
	MH	Ranganathan, Darshan et al., "Oxalo peptides as core motifs for protein design," J. Chem. Soc., 1993, (1), 92-4.
	MI	Dawson, Ted M. et al., "Immunosuppressant FK506 enhances phosphorylation of nitric oxide synthase and protects against glutamate neurotoxicity," Proc. Natl. Acad. Sci. USA, 1993, 90, 9808-12.
✓	MJ	Cunliffe, C. Jane et al., "Novel inhibitors of prolyl 4-hydroxylase. 3. Inhibition by the substrate analog N-oxaloglycine and its derivatives," J. Med. Chem., 1992, 35(14), 2652-8.
	MK	Waldmann, Herbert, "Amino acid esters as chiral auxiliaries in Barbier-type reactions in aqueous solutions," Liebigs Ann. Chem., 1991, (12), 1317-22. (German)
✓	ML	Krit, N.A. et al., "Impact of the nature of alkyl radical on the biological activity of N-carboxyalkyl dipeptides," Khim.-Farm. Zh., 1991, 25(7), 44-6. (Russian)
	MM	Blaschke et al., Chemical Abstracts, 1974, 85:78405k.

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	NB	4,310,461	1/12/82	Krapcho et al.			1/23/80
	NC	4,578,474	3/25/86	Krapcho et al.			11/19/84
	ND	4,531,964	7/30/85	Shimano et al.			8/29/83

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	NE	WO9535367	12/28/95	WO PCT			Yes
	NF	WO9413629	6/23/94	WO PCT			Yes

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<i>NG</i>	NG	Caufield, Craig E. and Musser, John H., "Macrocyclic Immunomodulators," <u>Annual Reports in Medicinal Chemistry</u> , Johns (Ed.), Academic Press, Chapter 21, 195-204, 1989.
<i>NH</i>	NH	Effenberger F. et al., "Diastereoselective addition of benzenesulfonyl chloride to 1-acryloylproline esters," <u>Chemical Abstracts</u> , 1989, 110:154846h.
<i>NI</i>	NI	Nakatsuka, M et al., "Total Synthesis of FK506 and an FKBP Reagent, (C <sub>8</sub> , C <sub>9</sub> - <sup>13</sup> C <sub>2</sub> )-FK-506," <u>J. Am. Chem. Soc.</u> , 1990, 112 (14), 5583-90..
<i>NJ</i>	NJ	Shu, A. et al., "Synthesis of I-125 labeled photoaffinity rapamycin analogs," <u>J. Labelled Compd. Radiopharm.</u> , 1996, 38(3), 277-37.
<i>NK</i>	NK	Tatlock, J. et al., "High affinity FKBP-12 ligands from (R)-(-)-carvone. Synthesis and evaluation of FK506 pyranose ring replacements," <u>Bioorg. Med. Chem. Lett.</u> , 1995, 5(21), 2489-94.
<i>NL</i>	NL	Teague, S. et al., "Synthesis of FK506-cylcosporin hybrid macrocycles," <u>Bioorg. Med. Chem. Lett.</u> , 1995, 5(20), 2341-6.
<i>NM</i>	NM	Stocks, M. et al., "Macrocyclic ring closures employing the intramolecular Heck reaction," <u>Tetrahedron Lett.</u> , 1995, 36(36), 6555-8.

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<i>n</i>	OA	4,390,695	1/28/83	Krapcho et al.			6/1/81
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	OD						

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<i>n</i>	OE	W09204370	3/19/92	USA PCT			Yes
<i>n</i>	OF	W09535308	12/28/95	WO PCT			Yes

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<i>n</i>	OG		Wang, C.P. et al., "High performance liquid chromatographic isolation and spectroscopic characterization of three major metabolites from the plasma of rats receiving rapamycin (sirolimus) orally," J. Liq. Chromatogr., 1995, 18(13), 2559-68.
	OH		Armistead, D.M. et al., "Design, synthesis and structure of non-macrocyclic inhibitors of FKBP12, the major binding protein for the immunosuppressant FK506," Acta Crystallogr. 1995, D51(4), 522-8.
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	OJ		Furber, Mark, "FKBP-12-ligand-calceineurin interactions: analogs of SBL506," J. Am. Chem. Soc., 1995, 117(27), 7267-8.
	OK		Chakraborty, TK et al., "Design and Synthesis of a rapamycin-based high affinity binding FKBP12 ligand," Chem. Biol., 1995, 2(3), 157-61.
<i>n</i>	OL		Wang, C.P. et al., "A high performance liquid chromatographic method for the determination of rapamycin (sirolimus) in rat serum, plasma, and blood and in monkey serum," J. Liq. Chromatogr., 1995, 18(9), 1801-8.
	OM		Smith, A.B. et al., "Total synthesis of rapamycin and demethoxyrapamycin," J. Am. Chem. Soc., 1995, 117(19), 5407-8.

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Examiner Initial		Document Number	Date	Name	Class	Sub-Class	Filing Date
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	PB						

**FOREIGN PATENT DOCUMENTS**

		Document Number	Date	Country	Class	Sub-Class	Translation
<i>MA</i>	PC	WO9221313	12/10/92	WO PCT			Yes
	PD	WO9524385	9/14/95	WO PCT	<del>X</del>		Yes

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<i>↑</i>	PE	Baumann, K. et al., "Synthesis and oxidative cleavage of the major equilibrium products of ascomycin and Fk 506," Tetrahedron Lett., 1995, 26(13), 2231-4.
	PF	Nelson, F. et al., "A novel ring contraction of rapamycin," Tetrahedron Lett., 1994, 35(41), 7557-60.
	PG	Dawson, T.M. et al., "The immunophilins, FK506 binding and cyclophilin, are discretely localized in the brain: relationship to calcineurin," Neuroscience, 1994, 62(2), 569-80.
	PH	Cameron, Andrew et al., "Immunophilin FK506 binding protein associated with inositol 1,4,5-triphosphate receptor modulates calcium flux," Proc. Natl. Acad. Sci. USA, 1995, 92, 1784-1788.
	PI	Stocks, M. et al., "The contribution to the binding of the pyranoside substituents in the excised binding domain of FK-506," Bioorg. Med. Chem. Lett., 1994, 4(12), 1457-60.
	PJ	Steiner, J.P. et al., "Nonimmunosuppressive Ligands for Neuroimmunophilins Promote Nerve Extension In Vitro and In Vivo," Society for Neuroscience Abstracts, 1996, 22, 297.13.
	PK	Lyons, W. Ernest et al., "Neronal Regeneration Enhances the Expression of the Immunophilin FKBP-12," The Journal of Neuroscience, 1995, 15, 2985-94.
	PL	Skotnicki, Jerauld et al., "Ring expanded rapamycin derivatives," Tetrahedron Lett., 1994, 35(2), 201-2.
<i>W</i>	PM	Skotnicki, Jerauld et al., "Synthesis of secorapamycin esters and amides," Tetrah. Lett., 1994, 35(2), 197-200.

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QB						

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QC	WO9307269	4/15/93	WO PCT			Yes
QD	WO9216501	10/1/92	WO PCT			Yes

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QE	Rao, A.V. Rama and Desibhatla, Vidyanand, "Studies directed towards the synthesis of rapamycin: stereoselective synthesis of C-1 to C-15 segment," Tetrahedron Lett., 1993, 34(44), 7111-14.
QF	Andrus, Merrit B., "Structure-based design of an acyclic ligand that bridges FKBP12 and calcineurin," J. Am. Chem. Soc., 1993, 115(2), 10420-1.
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QI	Nicolaou, K.C. et al., "Total Synthesis of rapamycin," J. Am. Chem. Soc., 1993, 115(10), 4419-20.
QJ	Hayward, C.M. et al., "Total Synthesis of rapamycin via a novel titanium-mediated aldol macrocyclization reaction," J. Am. Chem. Soc., 1993, 115(20), 9345-6.
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QL	Luengo, J. et al., "Studies on the chemistry of rapamycin: novel transformation under Lewis-acid catalysis," Tetrahedron Lett., 1993, 34(6), 991-4.

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RB						

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<i>✓</i>	RC <del>WO</del> 9526337	10/5/95	<i>WO</i> PCT		<i>+</i>	Yes

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<i>W</i>	RD		Yohannes, Daniel et al., "Degradation of rapamycin: retrieval of major intact subunits," Tetrahedron Lett., 1992, 33(49), 7469-72.
	RE		Goulet, Mark T. and Boger, Joshua, "Degradative studies on the tricarbonyl containing macrolide rapamycin," Tetrahedron Lett., 1991, 32(45), 6454.
	RF		Goulet, Mark T. et al., "Construction of the FK-506 analog from rapamycin-derived materials," Tetrahedron Lett., 1991, 32(36), 4627-30.
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	RH		Fisher, Matthew et al., "On the remarkable propensity for carbon-carbon bond cleavage reactions in the C(8)-C(10) region of FK-506," J. Org. Chem., 1991, 56(8), 2900-7.
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	RJ		Hayward, C.M. et al., "An application of the Suarez reaction to the regiospecific synthesis of the C <sub>28</sub> -C <sub>42</sub> segment of rapamycin," 3989-92.
	RK		Hovarth, R., et al., "An application of the Evans-Prasad 1,3-Syn diol synthesis to a stereospecific synthesis of the C <sub>10</sub> -C <sub>27</sub> segment of rapamycin," Tetrahedron Lett., 1993, 34(25), 3993-3996.
	RL		Whitesell, J.K. et al., "Asymmetric Induction. Reduction, Nucleophilic Addition to, Ene Reactions of Chiral $\alpha$ -Ketoesters," J. Chem. Soc., Chem Commun., 1983, 802.
<i>W</i>	RM		Ando, Takao et al., "Formation of Crossed Phenazine from the Reaction between Tetra-p-anisyl- and Tetra-p-tolyl-hydrazines in Liquid Sulphur Dioxide," Chem. Comm., S. Chem. Comm., 1975, 989.

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✓	SA	WO9219745	11/12/92	WO	PCT		Yes
	SB	WO9323548	11/25/93	WO	PCT		Yes
	SC	WO9636630	11/21/96	WO	PCT		Yes
	SD	WO9633187	10/24/96	WO	PCT		Yes
	SE	WO9633184	10/24/96	WO	PCT		Yes
	SF	WO9603318	10/24/96	WO	PCT		Yes
	SG	WO9820891	5/22/98	WO	PCT		Yes
	SH	WO9820892	5/22/98	WO	PCT		Yes
	SI	WO9820893	5/22/98	WO	PCT		Yes
✓	SJ	WO9824805	6/11/98	WO	PCT		Yes

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✓	SM	Steiner, Joseph P., et al., "Neurotrophic Immunophilin Ligands Stimulate Structural and Functional Recovery in Neurodegenerative Animal Models," 1997, Proc. Natl. Acad. Sci. USA, 94:2019-2024.
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<i>N</i>	UA	5,714,510	2-3-98	Proctor			6-5-95
	UB	5,620,971	4-15-97	Armistead et al.			3-25-94
	UC	5,472,687	12-5-95	Proctor			2-7-94
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	UG	EP 0823419	8-7-97	EPO			YES
	UH	EP 0519819	6-17-92	EPO			NO
	UI	EP 0494005	12-20-91	EPO			NO
	UJ	EP 0471135	8-14-90	EPO			YES
	UK	EP 0443983	12-2-91	EPO			NO
	UL	EP 0420707	8-24-90	EPO			NO
	UM	WO 9822432	5-28-98	WO			NO
	UN	WO 9813343	4-2-98	<i>WO</i> PCT			YES
	UO	WO 9731898	9-4-97	<i>WO</i> PCT			YES
	UP	WO 9611943	10-6-95	<i>WO</i> PCT			YES
	UQ	WO 9534303	12-21-95	<i>WO</i> PCT			YES
	UR	WO 9512398	5-11-95	<i>WO</i> PCT			YES
	US	WO 9502684	1-26-95	<i>WO</i> PCT			YES
	UT	WO 9403476	2-17-94	<i>WO</i> PCT			YES
	UU	WO 9318736	9-30-93	<i>WO</i> PCT			NO
	UV	WO 9314762	8-5-93	<i>WO</i> PCT			YES
	UW	WO 9314072	7-22-93	<i>WO</i> PCT			YES
	UX	WO 8906234	7-13-89	<i>WO</i> PCT			YES
<i>N</i>	UY	WO 8800040	1-14-88	<i>WO</i> PCT			YES

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